

THE QUESTION OF THE ANTI-TUBERCULAR  
POWER OF IODOFORM, WITH A SUGGES-  
TION FOR A MORE EXACT CLINI-  
CAL TESTING OF THE SAME.

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THE beneficial effect of iodoform when applied directly to tubercular tissues, has been widely accepted. This property was claimed for it by Mosetig v. Moorhof in his earliest publications on the subject of iodoform ("Versuche mit Iodoform als Wundverbandmittel nach Operationen wegen fungösen Prozesse."—*Wiener Med. Wochenschrift*, 1880, Nos. 43, 44, 46-49, 51; 1881, Nos. 13-41) and has been attested by many other clinicians, who, following his recommendation, put it to use.

At the French Congress for surgery in 1885 Verneuil made enthusiastic claims for this agent for the cure of cold abscesses by injections of ethereal solutions thereof, and he has repeatedly since, both in person and through his pupils, claimed specific curative powers for it in these tubercular diseases. Bruns and Nauwerk, in 1887, published a careful clinical and histological study of the effect of iodoform upon tubercular processes (*Beiträge zur Klin. Chirg.*, Bd. 3, hft. 1, s. 149), in which they claimed that under iodoform applications the bacilli disappeared from the tubercular granulation formation, that the further production of tuberculous tissue gradually ceased, that the already existing tubercular tissue became permeated and softened by a copious cell-exudation until, having become fatty and necrotic, it was pushed off by a healthy, very vascular, new granulation tissue, and that after the disappearance of the tubercle the vessels became obliterated, the granulations

shrank or became converted into connective tissue, the exudation ceased, the abscess contents became absorbed, and the walls finally adhered together by cicatricial formation. In the following year, 1888, Bruns again published a report on the subject (*Beiträge, etc.*, Bd. 4, hft. 1), in which the result of iodoform injections in the treatment of more than 100 cold abscesses is given. A large proportion of cures was obtained in these cases, usually after prolonged treatment, and the reporter claimed that the results were sufficient to warrant great encouragement to persevere in the iodoform treatment of such abscesses.

On the other hand Rovsing, in 1887 (*Fortschritte der Medicin*, 1887, 5, s. 257), reported the results of inoculation experiments made by him upon animals with tuberculous material rubbed up with iodoform. The inoculation of a small amount of tuberculous material rubbed up with a relatively considerable proportion of iodoform was followed in every case by an outbreak of local tuberculosis, after which general tuberculosis regularly developed. This local outbreak of tuberculosis was in no case hindered nor weakened by the effect of the iodoform, on the contrary in two cases in which at the same time iodoformized tubercle was inoculated in one eye, and pure tubercle in the other, the local tuberculous process showed itself several days earlier in the eyes into which the iodoformized tubercle had been inserted; these eyes also were more rapidly destroyed.

These results convinced this observer that iodoform has absolutely no influence on the vitality of tubercle bacilli; and have, still further, tended to develop a growing skepticism among surgeons in general as to any specific antitubercular power in this agent. Notwithstanding the vast mass of clinical evidence which had accumulated appearing to support such a claim for iodoform, the possibilities of error in accurately weighing the results of the use of any particular agent in the treatment of a diseased condition are so undeniable that this skepticism can be dispelled only by more exact evidence than has yet been accumulated, especially since the possibilities of spontaneous cure in many cases is becoming more fully appreciated, as the natural history of tuberculous processes is becoming more fully understood.

It is not to be gainsaid that great help in the successful treatment of local tuberculous affections has been obtained by the use of iodoform. How this has been accomplished is the question at issue. Have the good results obtained by clinicians been the result, then, of the general improvement in the methods of wound treatment, of which the use of iodoform has been only a part? May not equally good results be obtained by attention to these operative details without the use of iodoform? Some more recent observations published by Landerer, of Leipzig (*Münchener Med. Wochenschrift*, 1888, 40-41), in which he claims for balsam of Peru antitubercular powers which equal those claimed for iodoform, are susceptible of being made to support this last named hypothesis. The frequent cures of tubercular joint diseases, and the gradual disappearance of cold abscesses often obtained under simple rest, immobilization and general hygienic measures also present themselves as suggestive of doubt as to the specific antidotal effect of any particular drug. The occasional failures to favorably affect the condition of tuberculous foci, cavities, sinuses and ulcers by applications of iodoform likewise lend strength to one's skepticism as to its specific power, while finally, the now thoroughly demonstrated fact that iodoform has no power even to inhibit the growth of the common pyogenic micro-organisms, but on the contrary may be the medium of inoculating with septic organisms fresh wounds to which it may be applied, must unavoidably serve to still more strengthen any previously existing skepticism, or to awaken it if it is not already existing.

From the standpoint of the clinician a new series of experiments is now wanted, in each of which two lesions of identical character, similarly located in the body, with identical constitutional and hygienic conditions, shall be submitted by the same observer to treatment, the one by iodoform applications, the other by the use of any other means, exclusive of iodoform, that may commend itself to the judgment of the surgeon. By the comparison of the results of a considerable number of such tests a valuable check will be furnished to aid in an estimate of the value of the experience already accumulated in various ways. Such a series will also be in the same line with the

experimental work upon animals done by Rovsing, and will either corroborate the conclusions reached by this investigator or will serve to show that the condition which the surgeon has to cope with in the bodies of diseased men are different from those artificially produced in animals by the experimenter.

As a contribution to such a new series of experimental clinical observations, I desire to report the following case :

A girl, æt. 13 years, whose general health was good, and whose family history was free from tuberculosis, presented herself to me in November, 1888, with a peculiar infiltrated and ulcerated patch on either leg, and with a smaller patch of infiltration, not ulcerated, on the outer side of each thigh. The location of the affected areas was quite symmetrical as regards the two limbs. The patches on the legs were situated anteriorly just above the ankles. Their area was somewhat larger than that of a silver dollar; a well-defined margin circumscribed each patch; and their surfaces were irregularly eroded or honeycombed by small indolent ulcers having sharply defined overhanging borders, as if punched out and then undermined. More than three months had passed since the inception of the disease; the right ankle had been attacked first, after some time the left leg had developed the disease. Though under the treatment of an eminent specialist, no permanent improvement had been obtained, the history having been one of alternations of superficial healing and breaking down and slowly increasing infiltration. At the outset she had worn the usual garter encircling the leg above the knee; this was later replaced by elastics that passed upward on the outside of the thigh to be fastened at the waist. At the points where the greatest friction of these elastics against the outside of the thigh occurred the secondary infiltrated areas had developed. There were no varicose veins in either leg; there was no history of syphilis. The gross appearances of these various diseased patches warranted the provisional diagnosis of tuberculosis of the skin, and the opportunity which they presented to make comparative tests of treatment was taken advantage of. In the subsequent treatment the right leg patch was excised *en masse* by an incision which traversed apparently sound tissue both at its edges and underneath it. Subsequent examination of the part removed corroborated the diagnosis, many tuberculous nodules, pervaded by bacilli, being demonstrated throughout its central portion, especially in and about the ulcerated points. Beginning cheesy degeneration appeared in some of these nodules. The corium especially was the seat of these

changes. The general structure of the mass was loose and cedematous, being infiltrated with soft granulation tissue. The accompanying plate, Fig. 1, shows the histological appearances presented by this patch.

The first operative attack on the disease was made December 10, 1888, at which time the patches on the thighs were excised by an oval

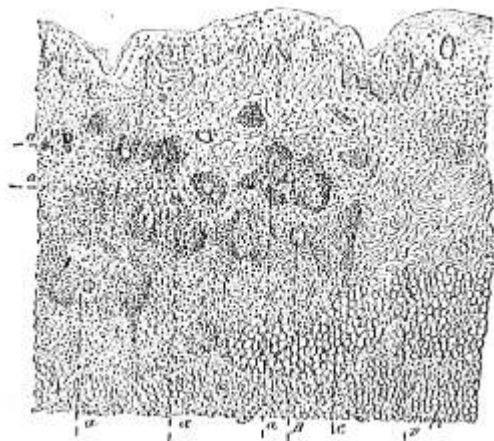


FIG. 1. SECTION SHOWING STRUCTURE OF TUBERCULAR ULCER OF LEG.

*a.* Panniculus adiposus.

*a.* Miliary tubercles.

*D.* Corium.

*B.* Giant cells in miliary tubercles.

incision. These wounds were sutured, primary union secured, and these points eliminated from further consideration. The diseased area on the right leg was also excised, as already stated, leaving an extensive surface to granulate. This was kept sprinkled over with powdered bisinuth and protected by an absorbent pad until the process of granulation was well established over its whole extent. This was somewhat slow in being secured, but finally at the end of six weeks, January 25, 1889, so firm and healthy a surface of granulations was presented by it that I attempted to secure its rapid and final healing by covering it with skin grafts, after the method of Thiersch. The immediate success of the attempt was complete, and at the end of a week definite healing of the whole seemed to have been accomplished. Soon, however, the new epithelial covering began to break down,

- point after point becoming necrotic and melting away, until at the end of two weeks more, bringing the history of the case up to February 13, it had largely disappeared, and an indolent ulcer, with flabby succulent granulations, had taken its place. It is important to note that at each point where the grafted skin first broke down, there was found in the tissues immediately underneath a little mass of bismuth which had evidently become covered in by the granulation tissue in the earlier course of the healing so deeply as to escape removal by the curette when the surface was finally scraped for the application of the grafts. With the shrinking and condensation of the tissues after the successful grafting these had become forced to the surface and had evidently so interfered with the nutrition of the overlying epithelium as to awaken a new ulcerative process.

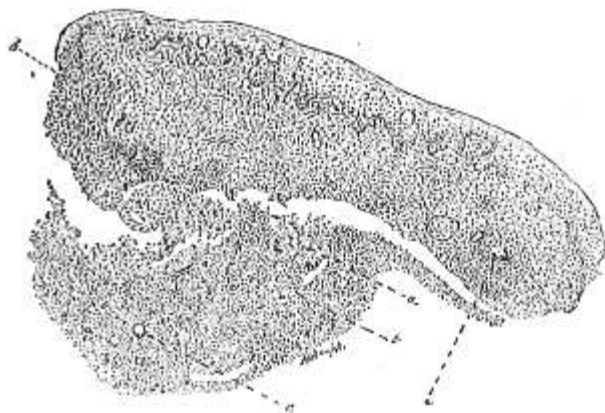


FIG. 2. SECTION SHOWING STRUCTURE OF BREAKING DOWN CICATRIN.

*From site of ulcer shown in Fig. 1 eight weeks after its excision.*

- a. Extravasated blood.
- b. Granulation tissue.
- c. Giant cells in granulation tissue.

The ulcer had now again the gross appearance of tubercular disease. I now curetted it thoroughly, with a view especially to remove all retained bismuth particles. I removed also a mass from its substance of sufficient size for the examination of the pathologist, Dr. Hodenpyl, who reported that though it was made up of poorly developed granulation tissue, containing in places giant and epithelioid cells,

and some aggregated masses of cells resembling tubercle tissue, repeated examinations for bacilli gave negative results. The accompanying plate, Fig. 2, shows the histological features of this section. A boracic acid ointment with occasional stimulation by nitrate of silver was ordered in the further treatment of the sore. At the end of another three weeks a steady but slow healing from the edges has been going on, but the process is tedious. The patient is unwilling to submit to any further curetting, or other operative procedure. Up to this time, a period of three months, no iodoform has been used upon this ulcer. It is now resorted to, March 8, by powdering it upon the granulating surface, and using an absorbent pad as a covering to the sore. After the lapse of six weeks more, when last examined, this sore is covered in over about two-thirds of its extent with a firm cicatrix, there still remaining a good sized, somewhat indolent granulating surface.

The ulcer upon the left leg was thoroughly curetted December 10, 1888, at the same sitting with the excision of its fellow on the right leg. The curetted surface was then sprinkled with iodoform and covered by an absorbent pad. Its further history is uneventful. The same method of dressing it was continued, the pads being changed and the sprinkling with iodoform being repeated every five or seven days. It rapidly healed by the extension of a soft firm cuticular covering from its margins. On January 25, while the patient was anaesthetised for the purpose of grafting the ulcer on the other leg, I took advantage of the opportunity to excise a wedge-shaped piece from the centre of the previously diseased area in the left leg, and submitted it to the pathologist for examination, who reported that it had the usual characteristics of primary cicatricial tissue, and was free from any evidence of tuberculosis. Recent examination of the site of this ulcer showed a firm soft natural skin to have been re-formed, presenting but slight traces of the former existence of any disease.

The difference in the course of these two ulcers was so marked that it could not escape the observation of even the most casual observer. The question as to the cause of this difference is singularly free from difficulty. The hygienic and constitutional and local conditions of these ulcers were the same for each, and unusually good for both. Both were treated at the same time and by the same surgeon. The difference in their course is unmistakably due to the difference in the treatment pursued. In this case certainly a most favorable influence

upon the tubercular process was exerted by the iodoform applications. Attention should not fail to be given, however, to the accessories of its employment. The grossly affected tubercular tissues were scraped away. By this proceeding the softer, more superficial layers only are removed, for no complete and radical removal of all infected tissue can be thus accomplished. What is done is to open up the deeper spaces and tissues so that they are readily permeated by the substance used for the dressings. I have in other cases repeatedly secured perfect and rapid healing by thoroughly cauterizing with the actual cautery the surface left by the curetting, and then applying a simple emollient salve. By the cautery the outlying infected tissue is destroyed and recurrence of the disease is guarded against. Although by the curette alone no assurance of complete extirpation can be secured, it still does aid materially in enabling the iodoform to be brought into immediate contact with the outlying loose tissues into which bacilli may have penetrated without yet having had time to provoke the development around them of proper tubercular tissue. The results obtained in the case detailed above apparently demonstrate a marked antitubercular effect from iodoform. The culture and inoculation experiments of Rovsing, DeRuyter, Neisser and others are sufficient to show that this effect is not a direct one. But it matters not whether this effect is a direct or an indirect one. If only a sufficiently extended and carefully guarded series of clinical tests can be made to demonstrate beyond a peradventure that the further activity of the bacilli of tuberculosis can be inhibited and the rapid restoration to a normal state upon the part of infected tissues can be secured by the proper use of iodoform, then no surgeon will refuse it a place among his resources as a most invaluable antitubercular agent.